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#### 1 SCOPE AND APPLICABILITY

- 1.1 This SOP establishes the requirements for conducting, reviewing and approving VA research submitted to the VA Central IRB that involves the use of vulnerable populations.
- 1.2 This policy applies to all VA Central IRB support staff, VA Central IRB members, investigators, and all project team members involved in research reviewed and approved by the VA Central IRB in which members of these vulnerable populations are participants.
- 1.3 The purpose of this policy is to describe the requirements for investigators to submit projects to the VA Central IRB that involve research with vulnerable populations and other special categories of research participants that may need additional safeguards.
- 1.4 It is the policy of the VA Central IRB that all projects it reviews involving vulnerable populations and other special classes of participants meet all VA and other requirements for such review and that additional protections and safeguards are considered for these populations as necessary to ensure that the principles of respect for persons, beneficence, and justice, as detailed in the Belmont Report are met. The VA Central IRB follows the policies on vulnerable populations as set forth in VHA Handbook 1200.05. The VA has not adopted regulations similar to 45 CFR 46 Subparts B through D.
- 1.5 In accordance with VA and other federal requirements, research participants considered categorically vulnerable include:
  - Pregnant women
  - Prisoners
  - Participants with impaired decision-making capacity
  - Children

Their involvement in a research project requires that the VA Central IRB make additional determinations to ensure adequate safeguards are included in the project by the investigators to protect the rights and welfare of these populations.

- 1.6 Other special categories of participants that may be potentially susceptible to undue influence or coercion and may require additional safeguards and protections of their rights and welfare include but are not limited to the following:
  - Participants who are illiterate or have limited or no English language proficiency
  - Students and employees of the VA
  - Terminally ill participants
  - Economically and/or educationally disadvantaged participants
- 1.7 The VA Central IRB will not approve any project in which a fetus, in-utero or ex-utero (including human fetal tissue), is a research subject nor will it approve any research related to *in vitro* fertilization.

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- Projects in which some or all of the participants are recruited from vulnerable populations as 1.8 described in paragraph 1.5 are initially reviewed by the convened VA Central IRB and are not reviewed under expedited review procedures, even if the project otherwise qualifies for expedited review with the following exceptions:
  - The use of pregnant women in minimal risk studies involving survey research or the completion of questionnaires or other minimal risk activity when pregnant women are not the focus of the research and there are no additional safeguards that must be taken to protect pregnant participants other than those for the general population.
  - The use of participants with impaired decision-making capacity in minimal risk studies involving survey research or the completion of questionnaires or other minimal risk activity when participants with impaired decision making capacity are not the focus of the research and no additional safeguards are required beyond ensuring that a Legally Authorized Representative is available to act on behalf of the participant.
- Populations listed in paragraph 1.6 may be reviewed using the expedited review process if the studies qualify. Upon the discretion of the Primary Reviewer and/or VA Central IRB Co-Chair the study can be referred to the convened IRB at any time during the review process.
- 1.10 It is the policy of the VA Central IRB that no individual, including vulnerable or other special categories of participants, should be prevented from having the opportunity to participate in approved human research unless such a category is otherwise prohibited from participating by VA or other requirements.

#### **DEFINITIONS** 2

- Ad Hoc Consultant refers to an individual with select competence in special areas invited by the VA Central IRB to review certain protocols based on a specific or unique expertise and to render an opinion or make recommendations to the VA Central IRB. These individuals may not vote on the project.
- Assent refers to a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative research, be construed as assent (45 CFR 46.402(a)). Any Aresearch, assent is also used in context with adults with impaired decision making capacity.
- Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46.402(a)).
- Cognitively Impaired refers to persons having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., dementia), or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain,

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terminally ill patients, and patients and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests (Office of Human Research Protections (OHRP) Guidebook, chapter 6, section D). For the purposes of this SOP, the phrase "impaired decision-making capacity," is synonymous with "cognitively impaired." Cognitive impairment may be temporary, permanent, or may fluctuate over time.

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- Fetus refers to the product of conception from the time of implantation until delivery (VHA 2.5 Handbook 1200.05).
- In vitro fertilization is any fertilization of human ova, which occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means (VHA Handbook 1200.05).
- Legally Authorized Representative (LAR) is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (38 CFR 16.102¢ and VHA Handbook 1200.05)
- Pregnancy refers to the period of time from implantation until delivery. (VHA Handbook 1200.05). 2.8
- **Prisoner** refers to any individual involuntarily confined or detained in a penal institution. The term is 2.9 intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing (VHA Handbook 1200.05).

#### RESPONSIBILITY

- The VA Central IRB Managers are responsible for ensuring that investigators complete and submit all required documentation and/or supplements if their project includes vulnerable populations and/or other special classes of participants. VA Central IRB Managers also assist Reviewers in determining whether the project must be reviewed at a convened meeting of the IRB or whether it can be reviewed using expedited review procedures.
- 3.2 The VA Central IRB Administrator is responsible for ensuring that a VA Central IRB member, or an ad hoe consultant who has experience with the defined vulnerable population or other special class of participants included in the project, is in attendance at the convened meeting when the project is reviewed. The VA Central IRB Administrator shares responsibility for scheduling or conducting specialized IRB training pertaining to specific research projects as needed when vulnerable subjects will be involved.
- VA Central IRB members are responsible for determining whether participants are capable of making an informed and independent choice about whether to participate in the project. If there are groups or individuals who may be subject to coercion or undue influence, or the participants have impaired decision-making capacity, the IRB must evaluate whether there are additional safeguards included in the research project and whether they are sufficient to protect the rights and welfare of the



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participants. The members will also ensure that the additional protections and safeguards reduce the potential for coercion or undue influence.

- 3.4 The VA Central IRB Co-Chairs share responsibility for requesting specialized training for the IRB members concerning a certain vulnerable population.
- 3.5 Investigators are responsible for completing the applicable vulnerable population supplement and submitting it with their project application package and/or including in the protocol any additional safeguards the VA Central IRB determines to be necessary to protect the vulnerable population to be used in the research.

#### 4 PROCEDURE

The following procedure describes the process for conducting, reviewing and approving VA research submitted to the VA Central IRB that involves the use of vulnerable populations. See a visual drawing of the process in **Attachment 1**, **VA Central IRB SOP 106 Process Chart**.

- 4.1 Receipt of a Project Application Involving a Vulnerable Population or Other Special Class of Participants.
  - 4.1.1 Upon receipt of a project application the VA Central IRB Manager notes while performing an administrative review whether the project involves the use of a vulnerable population. If it does, the VA Central IRB Manager verifies that the investigator included the pertinent supplement (VA Central IRB Form 110 series), if required, for that vulnerable population in the project documentation. This supplement is required if the project involves prisoners or participants with impaired decision-making capacity. If it is not included, the investigator is contacted and asked to complete it.
  - 4.1.2 If the project involves a special category of participants that may be potentially vulnerable as defined in paragraph 1.6, a separate vulnerable population supplement is not required. The VA Central IRB Manager and/or Reviewer verifies that safeguards and protections for these populations are included in the applicable portions of the VA Central IRB Form 108, Principal Investigator New Project Application.
  - 4.1.3 For all studies requiring review by the convened IRB, the VA Central IRB Administrator will ensure that a VA Central IRB member, or ad hoc consultant, who has expertise with the vulnerable population involved in the study will attend a meeting during which a study involving one of the following vulnerable populations is scheduled to be reviewed: pregnant women, prisoners, children, participants with impaired decision-making capacity, and economically and/or educationally disadvantaged participants.
- 4.2 <u>Research Involving Pregnant Women</u>. Whether a project can be reviewed using expedited review procedures, if it otherwise qualifies for expedited review, or whether it must be reviewed at the convened IRB depends upon whether pregnant women are the focus of the research.

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- 4.2.1 If pregnant women are the focus of the study or if any of the study interventions may affect the health or welfare of the either the mother or the fetus, the investigator must complete VA Central IRB Form 110a, Vulnerable Population Supplement (Pregnant Women)- Attachment 2 and the project must be reviewed by the convened IRB. The VA Central IRB uses this supplement and all the other documentation provided by the investigator to determine whether the additional safeguards included in the project are adequate to protect the participants' rights and welfare or whether additional safeguards are required for project approval.
- 4.2.2 If pregnant women are not the focus of a study and there are no additional safeguards required that would not apply to the rest of the study population, such as studies involving the completion of mail surveys or phone interviews, then the study may be reviewed under the expedited review process if it otherwise qualifies.
- 4.2.3 Women of child bearing potential may not be entered into studies involving the use of FDA Categories D or X drugs unless a waiver has been obtained from the CRADO.
- 4.3 Research Involving Prisoners. Research involving prisoners may not be conducted by VA investigators while on official duty, in VA facilities or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer (CRADO). The research proposed must meet one of the permitted research categories specified in 45 CFR 46 Subpart C 46.301 46.306(a)(2).
  - 4.3.1 If a project involves prisoners as participants, the investigator will complete VA Central IRB Form 110b, Vulnerable Population Supplement (Prisoners) (Attachment 3) and submit it the VA Central IRB along with the rest of the project documentation.
  - 4.3.2 When the convened IRB reviews research that involves prisoners as participants the following conditions must be met in order for the review to take place:
    - 4.3.2.4 One or more individuals who are prisoners or prisoner representatives must be at the convened meeting when the project is reviewed.
    - 4.3.2.2 A majority of the VA Central IRB members (exclusive of prisoner members) has no association with the prison involved, apart from their membership on the IRB.
  - 4.3.3 The VA Central IRB must verify that the biomedical or behavioral research involving prisoners as participants involves one or more of the criteria as specified in 45 CFR 46.306 for the use prisoners in human subjects research.
  - 43.4 The VA Central IRB may approve research involving prisoners only if it determines that all of the criteria as specified in 45 CDR 46.301 through 46.306 are met. The determinations made by the VA Central IRB are documented in the meeting minutes and the VA Central IRB decision document.

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- 4.3.5 If an investigator becomes aware of a participant who becomes a prisoner after enrollment, the investigator must notify the VA Central IRB immediately and the following actions must be taken:
  - 4.3.5.1 The Principal investigator must submit a written notification to the VA Central IRB Co-Chair. The notification must include a determination by the investigator that it would be in the best interest of the participant to remain in the study or that the participant can be safely withdrawn.
  - 4.3.5.2 The VA Central IRB Co-Chair may approve the continued participation if it is determined that the continued participation is in the best interest of the participant. If it is determined that the participant should continue in the study, the investigator must complete the VA Central IRB Form 110b and submit it as an amendment to the project, as well as apply to the CRADO for the required waiver. The amendment and all associated paperwork will be reviewed at a convened VA Central IRB meeting. The IRB will comply with 45 CFR 46.301-306 in performing the review.
- 4.3.6 If the research involving prisoners is supported in part by the Department of Health and Human Services, a copy of the proposal and the VA Central IRB decision documents will be express mailed to the Office of Human Research Protections (OHRP) for review.
- 4.3.7 The research may not proceed until the investigator has been notified that the VA Central IRB, OHRP if applicable, and the applicable local site Research and Development (R&D) offices have all approved the research
- 4.4 Research Involving Children. Research involving children must be carefully reviewed by the IRB for its relevance to the VA mission. The VA Central IRB must review and approve the project and certify that it involves no greater than minimal risk prior to a waiver being sought. The VA Central IRB does not review or approve research involving children who are wards as participants.
  - 4.4.1 The VA Central IRB reviews any project that involves children as research participants in accordance with 45 CFR 46, Subpart D and 21 CFR Part 50, Subpart D. Any project that the VA Central IRB determines involves greater than minimal risk to children as participants will not be approved. VA Central IRB determinations are documented in the minutes.
  - 4.4.2 No vulnerable population supplement is required. However, the VA Central IRB will ensure that requirements for permission by parents or guardians and for assent by children are in accordance with Subpart D regulations, and as is determined by state or local law for the jurisdiction in which the research will take place.
    - 4.4.2.1 In determining whether children are capable of assenting, the VA Central IRB shall take into account the ages, maturity and psychological state of the children involved. If the VA Central IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, the assent of the

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children is not a necessary condition for the approval and conduct of the research. Additionally, even where the VA Central IRB determines that the children are capable of providing assent, it may still waive the assent requirement if **all** of the following conditions are met:

- The waiver of the assent requirement will not adversely affect the rights and welfare of the children:
- The research could not practicably be carried out without the waiver; and
- Whenever appropriate, the children will be provided with additional pertinent information after participation.
- 4.4.2.2 Where the VA Central IRB determines that assent is required, it shall determine whether and how the assent must be documented depending upon the age of the child and the design of the study.
- 4.4.2.3 The VA Central IRB may determine that the permission of one parent is sufficient for studies described at Subpart D, 46,404 and 46,405. For studies described at 46,406 and 46,407 permission by both parents is required. Permission by parents or guardian will be documented in accordance with VA Central IRB SOP 105, Informed Consent Requirements.
- 4.4.3 The VA Central IRB will closely review the site applications for all sites where research with children will be conducted to ensure that the site has appropriate facilities for caring for children as applicable.
- 4.4.4 A VA Central IRB member or ad hoc advisor having appropriate pediatric expertise must be present at the convened meeting of the VA Central IRB when any project involving children as research participants is reviewed.
- 4.5 Research Involving Participants with Impaired Decision-Making Capacity. In order for the research to be reviewed at a convened VA Central IRB meeting, there must be at least one member in attendance who has experience with the cognitively impaired and at least one member who has experience in the type of research being reviewed. One member may meet both requirements if qualified. VA Central IRB members are provided training related to specific research populations, such as persons with impaired decision-making capacity.
  - 4.5.1 For all projects involving participants with impaired decision-making capacity, even if these participants are not the focus of the study, the investigator must complete and submit VA Central IRB Form 110c, Vulnerable Population Supplement (Impaired Decision-Making Capacity) -Attachment 4 and submit it with the rest of the required project documents.
  - 4.5.2 Individuals who lack decision-making capacity may be enrolled in a study if all the criteria as specified in VHA Handbook 1200.05, paragraph 49d are met.



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- 4.5.3 If all the VHA Handbook 1200.05 criteria are met, the VA Central IRB may approve the inclusion of individuals in the research who lack decision-making capacity on the basis of the study team obtaining informed consent from the participant's legally authorized representatives. Before approving the study the VA Central IRB must consider the following and document its deliberations in the minutes:
  - Ensure the study includes appropriate procedures for respecting dissent by the participant
  - Consider whether or not the study needs to include procedures for obtaining assent
  - Determine whether any additional safeguards need to be used
- 4.5.4 Individuals who, because of a known condition, are at high risk for temporary or fluctuating decision-making capacity, must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual's ability to provide informed consent. This evaluation must be performed as described in the IRB approved protocol.
  - 4.5.4.1 If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a legally authorized representative must provided informed consent.
  - 4.5.4.2 If the subject regains decision-making capacity, the investigator or designee must repeat the informed consent process with the subject, and obtain the subject's permission to continue with the study.
  - 4.5.4.3 For studies involving individuals with temporary or fluctuating decision-making capacity, the VA Central IRB may give special consideration to continuing review timeframes and may require more frequent review.
- 4.5.5 An individual is presumed to have decision-making capacity unless any one or more of the following apply:
  - It has been documented by a qualified practitioner in the individual's medical record in a signed and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study. The qualified practitioner may be a member of the study team.
  - The individual has been ruled incompetent by a court of law
- 5.6 If there is any question as to whether or not a potential adult subject has decision-making capacity, and there is no documentation in the medical records or the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the study team) about the individual's decision making capacity and the results documented before proceeding with the informed consent process.

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- 4.5.7 If an individual with decision making capacity is enrolled in a study, the VA Central IRB in its review of the project determines whether an assent process is required. If required, the VA Central IRB determines whether the plan for assent is adequate. Even if the VA Central IRB does not require assent, no participant that does not give assent may be forced or coerced to participate, even if the legally authorized representative consents for the participant. Investigators should also explain the proposed research project to the prospective participant when feasible, even if the surrogate gives consent.
- 4.5.8 The VA Central IRB will also determine if the investigator has an adequate plan to determine how and by whom capacity to consent will be assessed in populations where it is likely that capacity is impaired.
  - 4.5.8.1 Procedures must describe how participant's representatives will be informed regarding their roles and obligations to protect incompetent participants or persons with impaired decision making capacity.
  - 4.5.8.2 Legally authorized representatives will be given descriptions of both the proposed research project and their obligations as the participant's representative. They will be told that their obligation is to try and determine what the participant would do if competent, or if the participant's wishes cannot be determined, what they think is in the best interest of the incompetent person.
- 4.6 Research Involving Other Special Classes of Participants. The VA Central IRB considers students, VA employees, patients for whom an investigator provides medical care, the economically and/or educationally disadvantaged; individuals who have limited or no English language proficiency, and the terminally ill, as potentially vulnerable participants since they may be susceptible to undue influence or coercion. The VA Central IRB also evaluates other populations where cultural differences may make them susceptible to undue influence or coercion, such as Native Americans.
  - 4.6.1 There is no additional vulnerable population supplement required by the VA Central IRB for these special classes. The VA Central IRB reviews the potential risks and benefits of each proposed project on a case-by-case basis with increased emphasis on possible safeguards that may need to be implemented to protect the participant's rights and welfare.
  - 4.6.2 The VA Central IRB has the following requirements when some or all of the participants fall into one of these special classes:
    - 4.6.2.1 <u>Students and Employees</u>. When directly solicited to participate in a project, the VA Central IRB will ensure the following safeguards are in place as applicable:
      - 4.6.2.1.1. Anyone with an employment or academic relationship to the VA will be informed that their participation in the project, or refusal to do so, will in no way influence their employment, ratings, or subsequent recommendations. The involvement of students or employees in the project requires a disclosure in the informed consent form



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acknowledging that refusal to participate will have no influence on their academic progress or employment status.

- 4.6.2.1.2 The VA Central IRB will ensure that students and employees are not subject to undue influence or coercion. The relationship of the investigators to employee participants will be reviewed and safeguards required as applicable to ensure supervisors do not unduly influence potential participants.
- 4.6.2.1.3 For studies involving VA employees, Unions may need to be informed of the study. This is a local site issue. The VA Central IRB will include a reminder note in the study approval letter to the Principal Investigator that the local Research Office will need to be consulted in regard to local procedures for contacting the Union about potential research projects in which VA employees may be involved.
- 4.6.2.2 <u>Illiterate Participants and Literate Participants Who Cannot Sign the Informed Consent Document</u>. If the use of illiterate participants is proposed, or participants who are literate but cannot physically sign the consent document, the investigator will provide details on how the informed consent is going to be obtained.
  - 4.6.2.2.1 For illiterate participants, at a minimum, the investigator will include in the description that the informed consent document is read to the participant and the document then signed by the participant in the signature section by the participant "making their mark" and how this was done. The VA Central IRB requires both a witness to the mark and the person conducting the consent also sign and date the consent form.
  - A similar process is followed for potential participants who are literate and mentally capable of giving informed consent but physically unable to sign the form. The VA Central IRB can add additional stipulations depending upon the capabilities of the study population and the research design.
    - The investigator must specify on the Local Site Investigator Application if there are any state and local laws that govern how an illiterate subject is to "make their mark" or how a literate person who cannot physically sign the form, indicates consent if this differs from that approved as part of the PI Application.
- 4.6.2.3 Non-English Speaking Participants. Most VA research involves Veterans as subjects. Veterans by the nature of their service are deemed to be proficient in English but exceptions may apply and will be considered by the VA Central IRB as applicable, such as older Veterans residing in Spanish-speaking areas, i.e., Puerto Rico.



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- 4.6.2.3.1 If the involvement of participants who do not speak or read English is proposed (this would mainly involve family members of Veterans), a translator will be present to assist in the consent process and act as witness. A professional translator is preferred. In no case should the translator be a family member of the prospective subject.
- 4.6.2.3.2 Consent documents will be written in a language understandable to the participant population and a copy of the translated document forwarded to the VA Central IRB for review prior to enrollment of any participants. The VA Central IRB may use the expedited review procedure in reviewing this document if the English language version has already been approved and the translation is done by a certified translator.
- 4.6.2.3.3 Other situations will be reviewed on a study by study basis.
- 4.6.2.4 <u>Investigator is Participant's Medical Provider</u>. For projects in which an investigator also serves as one of the potential participant's health care provider, someone other than the investigator will be designated to obtain the informed consent. Potential participants must be informed in the consent document that refusal to participate will in no way affect their current or future treatment.
- 4.6.2.5 <u>Educationally or Economically Disadvantaged Participants</u>. The VA Central IRB will consider the following as applicable:
  - 4.6.2.5.1 For educationally disadvantaged participants, the VA Central IRB may require investigators to include in the project a method for the participants to demonstrate their understanding of the risks and benefits involved, such as answering questions or filling out a questionnaire to determine if they understood the concepts relayed.
  - 4.6.2.5.2 For potential participants who are economically disadvantaged, the VA Central IRB will pay particular attention to any payment that may be offered for participation in the project to ensure it is reasonable and of such a nature that it would not be a factor in causing an undue influence on the participant.
- 1.6.2.6 Terminally Ill Participants. Terminally ill patients may be considered a special class of participants that may be subject to undue influence or coercion based on their lack of alternatives. Investigators will ensure that the nature, magnitude, and probability of the risks and benefits of the research are identified as clearly and as accurately as possible. Accurate information concerning eligibility for participation, treatment options, and risks and benefits will be conveyed clearly and in a manner that will not either engender false hope or eliminate all hope.

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- 4.6.3 Although participants may not be considered a vulnerable population or special class of participants in federal regulations, the VA Central IRB require additional protections for certain participants based on the design of a particular study. If this determination is made, it will be documented in the minutes and the project approval letter.
- 4.7 <u>Additional Safeguards</u>. After reviewing a project, the VA Central IRB may require additional safeguards to protect the rights and welfare of the participants. Some of these measures may include but are not limited to the following:
  - 4.7.1 Require a reduction in payment or a change in the form of payment given.
  - 4.7.2 Involvement of family members and caregivers in the consent process and/or a requirement for periodic re-consent.
  - 4.7.3 Require third-party consent monitors during the recruitment and consenting process.
  - 4.7.4 Require longer waiting periods between the consent process and signing the consent document.
  - 4.7.5 Repeated consent sessions with groups of participants and/or the use of audiovisual aids.
  - 4.7.6 More frequent continuing review cycles.
- 4.8. <u>Participation in Multiple Studies</u>. <u>Dual enrollment</u>, i.e., enrollment in two or more studies concurrently, may be permitted as long as the dual enrollment:
  - Does not adversely affect the rights or well-being of the subject; or
  - Is not prohibited by the funding agency (e.g., CSP) or by one or more of the studies.

It is the responsibility of the Principal Investigator or Local Site Investigator to determine if it is appropriate for a subject to be in more than one study concurrently. This may require, especially for clinical studies, contacting the Principal Investigator of the other study to determine appropriateness.

#### 5 DOCUMENTATION REQUIREMENTS

- 5.1 The following are documentation requirements concerning the use of vulnerable and special categories of participants:
  - 5.1.1. The VA Central IRB will document its review of safeguards and that the use of a particular vulnerable population or special category of participant as applicable is approved in the final project approval letter for all projects and in the VA Central IRB minutes as applicable for studies reviewed at the convened IRB.
  - 5.1.2 Reviewers will complete applicable portions of Reviewer Checklists for all special or vulnerable populations proposed for use in a study.



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5.1.3 Investigators will complete the applicable Vulnerable Population Supplement (See Attachments 2, 3 and 4), as well as the applicable sections of the VA Central IRB Form 108 concerning the proposed use of these populations and the safeguards to be employed. In addition, the protocol must contain this information as well.

#### 6 REFERENCES

- 6.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects
- 6.2 VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research
- 6.3 45 CFR 46, Department of Health and Human Services, Protection of Human Subjects
- 6.4 VHA Directive 2001-028, Research Involving Children
- 6.5 Institutional Review Board Guidebook (OHRP)

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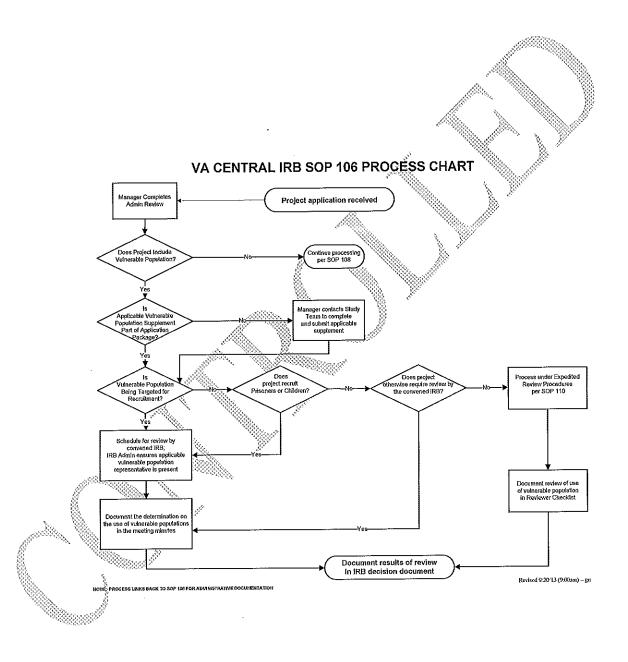
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#### Attachment 1





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#### Attachments

- 2. VA Central IRB Form 110a, Vulnerable Population Supplement (Pregnant Women) https://vaww.ord.portal.va.gov/sites/comm/admin/quality/default.aspx
- 3. VA Central IRB Form 110b, Vulnerable Population Supplement (Prisoners) https://vaww.ord.portal.va.gov/sites/comm/admin/quality/default.aspx
- 4. VA Central IRB Form 110c, Vulnerable Population Supplement (Impaired Decision-Making Capacity)

https://vaww.ord.portal.va.gov/sites/comm/admin/quality/default.aspx



## Vulnerable Population Supplement (Pregnant Women)



This form must be included with all project applications that target pregnant women for recruitment, for studies in which the risk level is greater that minimal and pregnant women are not excluded, or for any project in which there may be increased risk to the mother or fetus due to study interventions or procedures.

| I. Stud  | dy Identification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |        |     |
|----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------|-----|
| Title of |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |          |        |     |
| Princip  | al                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |        |     |
|          | gator/Study Chair                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ··-      | ····   |     |
| II Pos   | quirements for the Use of Pregnant Women in Research                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |          |        |     |
| The inv  | restigator must provide a response for each question or statement                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | YES      | NO     | N/A |
| below.   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |          |        |     |
|          | Are pregnant women the focus of the research? If yes, all of the following questions or statements must be answered yes. If no, skip to question 9.                                                                                                                                                                                                                                                                                                                                                                                                                    |          |        |     |
| 2.       | Where scientifically appropriate, have preclinical studies including studies on pregnant animals and clinical studies including studies on non-pregnant women, been conducted and do they provide data for assessing potential risks to pregnant women and fetuses? A description of such studies should be included in the project application.                                                                                                                                                                                                                       |          |        |     |
| 3.       | The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important medical knowledge which cannot be obtained by any other means.                                                                                                                                                                                           |          |        |     |
| 4        | If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the pregnant woman's informed consent is obtained in accordance with the informed consent provisions of 38 CFR 16.116, paragraphs 30-35 and 45 CFR 46.204(d). |          |        |     |
| 4.       | Each individual providing informed consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus.                                                                                                                                                                                                                                                                                                                                                                                                                                 |          | -      |     |
| 5.       | Is any risk the least possible for achieving the objectives of the research?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |          |        |     |
| 6.       | There are no inducements included in the research, monetary or otherwise, that will be offered to terminate a pregnancy.                                                                                                                                                                                                                                                                                                                                                                                                                                               |          |        |     |
| 7.       | Individuals involved in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.                                                                                                                                                                                                                                                                                                                                                                                                                         |          |        |     |
| 8.       | Individuals engaged in the research will have no part in determining the viability of a neonate.                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |        |     |
| 9        | Describe any additional protections and safeguards in the protocol for the u women:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | se of pr | egnant |     |

| e prin | cipal investigator must check each box and sign and date the form.                                                                                                                                                                                                                                      |
|--------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|        | I understand my responsibilities to follow all applicable VA And federal requirements to protect the rights and welfare of this vulnerable population.                                                                                                                                                  |
|        | I understand that the informed consent requirements described in VHA Handbook 1200.05 concerning this vulnerable population are not intended to preempt any applicable federal, state, or local laws that require additional information be disclosed for the informed consent to be legally effective. |
|        | I agree to follow all additional protections and safeguards for this vulnerable population as described in this project and as required by the VA Central IRB and I will ensure my project team is informed of these protections, safeguards, and requirements.                                         |

## Vulnerable Population Supplement (Prisoners)

I. Study Identification



This form must be included with all project applications that involve prisoners as potential participants or be submitted with a Request for an Amendment if a subject becomes a prisoner during the course of the study and it has been determined it is in the best interest of the subject to be continued on the study.

| Title of Study                                                                                                                      |                                                                                                                                                                                                                                          |                                       |          |      |
|-------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|----------|------|
| Principal Investigator                                                                                                              |                                                                                                                                                                                                                                          | · · · · · · · · · · · · · · · · · · · |          |      |
| II. Protections and Safe                                                                                                            | eguards Included in the Project                                                                                                                                                                                                          |                                       |          |      |
| The investigator must provi<br>below. All responses must                                                                            | de a response for each question or statement<br>be answered as "Yes" or "N/A" if this vulnerable<br>I as participants in the project.                                                                                                    | YES                                   | NO       | N/A  |
| Are there any possible participation in the resconditions, medical capacity armings in the prison.                                  | e advantages to the prisoner from his/her search when compared to the general living are, quality of food, amenities, and opportunity for that would impair the participant's ability to weigh act against the value of such advantages? |                                       |          |      |
| <ol><li>Are the risks involved</li></ol>                                                                                            | in the research commensurate with the risks that non-prisoner volunteers?                                                                                                                                                                |                                       |          |      |
| Are procedures for se<br>prisoners and immun<br>are these procedures                                                                | election of participants within the prison fair to all e from arbitrary intervention by prison authorities and described in the project?                                                                                                 |                                       |          |      |
| If control groups are quantities are quantities are quantities.  4. If control groups are quantities are quantities are quantities. | going to be used, will the control participants be                                                                                                                                                                                       |                                       |          |      |
| 5. Is the information pre prison population?                                                                                        | sented in a language understandable to the general                                                                                                                                                                                       |                                       |          |      |
| <ol><li>Does the informed co</li></ol>                                                                                              | nsent document clearly state that participation in the ct parole decisions and has the investigator trained his requirement?                                                                                                             |                                       |          |      |
| 7. If there is a need for the end of their partic made for such exami individual prisoner se                                        | follow-up examinations or care of participants after ipation in the research, has adequate provision been nations or care considering the length of the ntences and are these provisions described in the                                |                                       |          |      |
| If additional protections and s detail them below.                                                                                  | afeguards are included in the project and are not desc                                                                                                                                                                                   | ribed at                              | ove, ple | ease |
| Gottili Biolif Bolow.                                                                                                               |                                                                                                                                                                                                                                          |                                       |          |      |
|                                                                                                                                     |                                                                                                                                                                                                                                          |                                       |          |      |
|                                                                                                                                     |                                                                                                                                                                                                                                          |                                       |          |      |
|                                                                                                                                     |                                                                                                                                                                                                                                          |                                       |          |      |
|                                                                                                                                     |                                                                                                                                                                                                                                          |                                       |          |      |
|                                                                                                                                     |                                                                                                                                                                                                                                          |                                       |          |      |

| The research is minimal risk and no more than an inconvenience to the participants. It involves the possible causes, effects, and processes of incarceration and of criminal behavior.                                                                                                                                                                                                                                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The research is minimal risk and no more than an inconvenience to the participants. It involves a study of prisons as institutional structures or of prisoners as incarcerated persons                                                                                                                                                                                                                                                                          |
| The research is a study on conditions particularly affecting prisoners as a class, i.e., social and psychological problems such as alcoholism and drug addiction.                                                                                                                                                                                                                                                                                               |
| The research is a study on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health and/or well being of the participants.                                                                                                                                                                                                                                                                             |
| This is an epidemiologic study. The sole purpose of the project is to describe the prevalence or incidence of a disease or condition by identifying all cases or to study the potential risk factors associated with a disease or condition. The research presents no more than minima risk and no more than an inconvenience to the participants. Prisoners are not a particular focus of the research.                                                        |
| The research involves a project participant that became incarcerated after enrollment in the Project. It is to the benefit of the project participant to remain enrolled in the project. If yes, please justify:                                                                                                                                                                                                                                                |
| estigator Certification<br>cipal investigator must check each box and sign and date the form.                                                                                                                                                                                                                                                                                                                                                                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| I understand my responsibilities to follow all applicable VA and federal requirements to protect the rights and welfare of this vulnerable population.                                                                                                                                                                                                                                                                                                          |
| I will ensure all the project team members are trained in the additional protections and safeguards that are to be afforded this vulnerable population as stipulated in this supplement and as may be further mandated by the VA Central IRB.                                                                                                                                                                                                                   |
| I understand that I must receive a waiver from the Chief Research and Development Officer per VHA Handbook 1200.05 for conducting research with prisoners as participants after I have obtained approval from the VA Central IRB and the local R&D committees prior to beginning any research on prisoner participants. The only exception is if the VA Central IRB Co-Chair approves the continued participation of a participant who becomes a prisoner after |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

Signed

Date

# Vulnerable Population Supplement (Individuals with Impaired Decision-Making Capacity)



This form must be included with all project submissions unless individuals with impaired decision making capacity are excluded from the study.

| I. Study Ide                   | entification                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                  |  |  |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|
| Title of Study                 | ly                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                  |  |  |
| Principal Inve                 | Principal Investigator                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                  |  |  |
| II. Eligibility for Enrollment |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                  |  |  |
| The investiga                  | ator must check                                                                                                                                                                                                                                                                                                           | the applicable boxes as indicated.                                                                                                                                                                               |  |  |
| a. The propo                   | sed research e                                                                                                                                                                                                                                                                                                            | ntails one of the following:                                                                                                                                                                                     |  |  |
|                                | No greater tha                                                                                                                                                                                                                                                                                                            | n minimal risk to the subject.                                                                                                                                                                                   |  |  |
|                                | The research presents some probability of harm but there is a greater probability of direct benefit to the participant.                                                                                                                                                                                                   |                                                                                                                                                                                                                  |  |  |
|                                | The research is greater than minimal risk and there is no prospect of direct benefit to individual subjects but the research is likely to yield generalizable knowledge about the subjects disorder or condition that is of vital importance to the understanding or amelioration of the subject's disorder or condition. |                                                                                                                                                                                                                  |  |  |
| b. Please che<br>decision-r    | eck which of th<br>making capacity                                                                                                                                                                                                                                                                                        | e following requirements for the inclusion of individuals with impaired is met by your study purpose and design.                                                                                                 |  |  |
|                                | or not the lack                                                                                                                                                                                                                                                                                                           | eading to the subject's decision-making capacity is being studied, whether of decision-making capacity itself is being evaluated, but only if the study ormed with only persons having decision-making capacity. |  |  |
|                                | capacity, but a                                                                                                                                                                                                                                                                                                           | the study is not directly related to the individual's lack of decision-making compelling argument can be made for including individuals who lack ag capacity in the study.                                       |  |  |
| Provide justi                  | fication for the                                                                                                                                                                                                                                                                                                          | box you checked above:                                                                                                                                                                                           |  |  |
|                                |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                  |  |  |
|                                |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                  |  |  |
|                                |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                  |  |  |

| III. Addit          | ional Safeguards                                                                                                                                                                                |                                                                            |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Please ans          | wer the following questions regarding additional safegua<br>t of this population.                                                                                                               | ards and protections for the                                               |
|                     | a description in your protocol detailing how an indiv<br>ned prior to enrolling the participant in the study?                                                                                   | vidual's decision-making capacity is                                       |
| ☐ Yes               | No. If no, specify what the plan is:                                                                                                                                                            |                                                                            |
|                     | e protocol contain provision for obtaining assent of<br>of the participant?                                                                                                                     | the participant and to respect any                                         |
| ☐ Yes               | ☐ No. If no, specify what the plan is:                                                                                                                                                          |                                                                            |
| represe<br>providir | e protocol detail adequate provisions for informing to the roles and responsibilities of the legally gethe legally authorized representative with all the indicate to the participant?          | authorized representative and for                                          |
| ☐ Yes               | ☐ No. If no, specify what the plan is:                                                                                                                                                          |                                                                            |
|                     | e study involve participants with temporary or fluctu                                                                                                                                           | uating impaired decision-making                                            |
| ☐ Yes               | ☐ No                                                                                                                                                                                            |                                                                            |
|                     | there a plan for re-consenting subjects detailed in the pr<br>making capacity?                                                                                                                  | otocol after the participant regains                                       |
| ☐ Yes               | No. If no, specify what the plan is:                                                                                                                                                            |                                                                            |
| e. Please           | provide information on any additional safeguards inc<br>nerable population:                                                                                                                     | cluded in the protocol to protect                                          |
| IV. Inves           | tigator Certification                                                                                                                                                                           |                                                                            |
| The princ           | ipal investigator must check each box and sign and                                                                                                                                              | date the form.                                                             |
|                     | I understand my responsibilities to follow all applicable protect the rights and welfare of this vulnerable populati                                                                            |                                                                            |
|                     | understand that the informed consent requirements deconcerning this vulnerable population are not intended state, or local laws that require additional information be to be legally effective. | scribed in VHA Handbook 1200.05 to preempt any applicable federal,         |
|                     | understand VHA Handbook 1200.05 describes the enticonsent for research purposes unless otherwise specific                                                                                       | ed by applicable state law.                                                |
|                     | agree to follow all additional protections and safeguard<br>described in this project and as required by the VA Cent<br>team is informed of these protections, safeguards, and r                | Is for this vulnerable population as tral IRB and I will ensure my project |
|                     |                                                                                                                                                                                                 |                                                                            |
|                     | Signed                                                                                                                                                                                          | Date                                                                       |